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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,351	06/07/2002	Stace Lindsay	06727/008002	8638
21559	7590	10/31/2005	EXAMINER	
CLARK & ELBING LLP			BERTOGGIO, VALARIE E	
101 FEDERAL STREET			ART UNIT	
BOSTON, MA 02110			PAPER NUMBER	

1632

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/030,351

Applicant(s)

LINDSAY ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 2, 4, 8, 9 and 12-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 5-7, 10 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 05/05/2003
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's reply dated 09/26/2005 has been received. Claims 5,7,10 and 11 have been amended. Claims 2,4,8,9 and 12-20 are withdrawn. Claims 1-20 are pending and claims 1,3,5-7,10 and 11 are under consideration in the instant office action.

Specification

The objection to the disclosure is withdrawn in light of Applicant's amendment to the specification.

Claim Objections

The objection to claim 11 is withdrawn in light of Applicant's amendment to the claim.

Claim Rejections - 35 USC § 112-1st paragraph

1) The rejection of claims 3,5 and 7 under 35 U.S.C. 112, first paragraph, as lacking enablement is withdrawn in light of Applicant's amendments to the claims. However, claims 10 and 11 remain rejected as set forth below.

Claims 10 and 11 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a rHuAFP that is secreted in the milk of a transgenic non-human mammal wherein the non-human mammal is made by introducing the transgene into cells of an embryo and for a method of producing a rHuAFP that is secreted in the milk of a transgenic mouse wherein the mouse is made by introducing the transgene into cells of an embryo or into mouse ES cells, does not reasonably provide enablement for any such mammal made using any cell type or a transgenic human made using

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any method. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is maintained for reasons of record set forth at pages 4-8 of the previous office action dated 03/22/2005.

Applicant's arguments have been fully considered and are partially persuasive.

Applicant has amended claims such that they no longer read on chimeric animals.

Therefore, this aspect of the rejection is withdrawn.

However, claims 10 and 11 continue to encompass use of any transfected cell type to make an animal (see paragraph bridging pages 5-6 of the previous office action dated 03/22/2005). As set forth at pages 6-7 of the office action dated 03/22/2005, the state of the art at the time of filing held that it was routine to make transgenic non-human mammals using only fertilized oocytes or embryos that are transfected with a transgene, with the exception of transgenic mice, that can be made using totipotent ES cells. The state of the art of somatic cell nuclear transfer to generate a non-human animal was highly unpredictable as to the rate of success of making an animal, irrespective of transgene insertion or expression (see page 8 of the previous office action dated 03/22/2005).

Thus, the claims encompass use of any transfected cell to make a non-human mammal, which was not enabled by the specification or the art at the time of filing. Applicant has argued that several transgenic mice and goats that are capable of secreting rHuAFP into their milk have been made using techniques known in the art and taught in the specification.

In response, the specification merely mentions the use of nuclear transfer to make the claimed non-human mammals. The specification teaches making transgenic goats that secrete

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rHuAFP into the milk by injection of fertilized oocytes (pages 16-17), which was well-established and routine in the art at the time of filing. The specification does not describe in a manner that would enable one of routine skill in the art, how to carry out the methods of claims 10 and 11 using somatic cell nuclear transfer. Nuclear transfer was a highly underdeveloped art at the time of filing. As set forth at page 8 of the previous office action dated 03/22/2005, the first attempt at expressing a protein in the milk of a transgenic goat generated through nuclear transfer was reported in the art in May 1999, after the effective filing date of the instant application of 01/06/1999. Also as set forth at page 8 of the previous office action dated 03/22/2005, the state of the art of somatic cell nuclear transfer was highly unpredictable. The mere mention in the specification of using this technology does not overcome the underdeveloped and unpredictable nature of the art in such a way as to enable the ordinary skilled artisan to carry out the claimed method. While Applicant argues that mice and goats were made using the techniques described in the specification, it is noted that the specification described making goats through oocyte injection, which is applicable and enabling for other non-human mammals. The specification in combination with the art at the time of filing provided the necessary techniques necessary to make transgenic mice secreting rHuAFP in the milk by use of either ES cells in mice or injection of oocytes for other non-human mammals. Thus, the scope of the claims should be limited accordingly.

The declaration under 37 CFR 1.132 filed 09/26/2005 is insufficient to overcome the rejection of claims 10 and 11 based upon the insufficiency of disclosure under 35 U.S.C. 112, first paragraph as set forth in the last Office action because: The declaration is unsigned.

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Because the submission is unsigned, it is not considered to be a declaration and the evidence provided therein has not been considered.

The aspect of the rejection pertaining to nuclear transfer to make transgenic humans is withdrawn in light of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's amendment to the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1,3,5-7,10 and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Deboer (1997, US 5,633,076; IDS) or Clark (1994, US 5,322,775;IDS) or Lubon (1998, US 5,831,141; IDS) in view of Morinaga (1983, PNAS, Vol. 80, pages 4604-4608; IDS) and Bennett (1997, Breast Cancer Research and Treatment, Vol. 45, pages 169-179; IDS) for reasons of record set forth at pages 10-13 of the previous office action dated 03/22/2005.

Applicant argues that neither Deboer, Clark nor Lubon teach using transgenic technology to make rHuAFP. Applicant argues that while Morinaga taught the DNA sequence encoding HuAFP, Morinaga did not provide motivation to combine the teachings of Deboer, Clark or Lubon with that of HuAFP to produce and secrete HuAFP in the milk of transgenic mammals (see pages 12-15 of Applicant's Remarks). Applicant admits that Bennett concluded the need for large quantities of rHuAFP to facilitate further study of the therapeutic potential of rHuAFP as a regulator of breast cancer (see Remarks at page 14, paragraph 2). Applicant argues that Morinaga and Bennett did not teach the combination of DNA sequences required by the claims and that Bennett is limited to teaching expression of rHuAFP in *E.coli*. Applicant argues that the cited references fail to provide suggestion, motivation or teaching to express rHuAFP in the milk of a transgenic non-human mammal when none of the reference discuss or mention Applicant's specific combination in a way that would lead to Applicant's invention (page 15, paragraph 2) and suggests that the statement of obviousness is based on hindsight reasoning.

In response, it was the general state of the art as demonstrated by DeBoer, Clark and Lubon to use a transgenic non-human mammal as a bioreactor to produce large quantities of any protein of interest. The only elements lacking from any of these references, alone or in combination, is the sequence encoding AFP and motivation to use the sequence in the techniques

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of any of DeBoer, Clark or Lubon. Other required elements of transgene structure were known in this art including milk-specific promoters and leader sequences as they were necessary for and taught by DeBoer, Clark and Lubon. While the teachings of Bennett may be limited to producing rHuAFP using *E. coli*, no more is necessary. Bennett is relied upon solely for the motivation to apply the teachings of DeBoer, Clark or Lubon to the teaching of Morinaga of the AFP gene sequence. In summary, DeBoer, Clark and Lubon each taught the claimed nucleic acid as it relates to other proteins of interest, and taught the transgenic non-human mammal and methods as they relate to other proteins of interest; Bennett provided the motivation that made AFP a protein of interest; Morinaga taught the AFP gene sequence necessary to apply the techniques of DeBoer, Lubon and Clark to fulfill the motivation of Bennet.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Thus, the claimed invention, as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

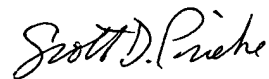
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
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SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER